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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,310	03/14/2001	Samir Khleif	15280415100	9099

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/810,310	KHLEIF ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-8 and 11-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-8 and 11-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and response filed 8/10/04 is acknowledged and has been entered.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 2, 6-8 and 11-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed method for eliciting an immune response in a subject comprising administering any peptide or protein antigen, including those recited in the instant claims and including from HIV proteins, and further comprising one or more T cell epitopes coordinately with a non-viral vector comprising a polynucleotide encoding a B7 co-stimulatory molecule, including those antigens, polynucleotides and vectors such as naked DNA vector, recited in the instant claims.

The instant claims encompass use of nucleic acid molecules, polynucleotides, encoding B7 co-stimulatory molecules and further comprising any peptide or protein antigens to elicit an immune response in a subject. There is insufficient disclosure in the specification on such a method as claimed in the instant claims.

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

The specification discloses that a secondary "co-stimulation" signal is required for optimal stimulation and effective antigen specific clonal expansion of lymphocytes in addition to a primary antigen specific signal, and that a two signal model has been proposed for all lymphocytes (page 3 at lines 14-19). The specification discloses that the primary activation signal typically involves an antigenic peptide bound to either class I or class II MHC (page 3 at lines 20-22). The specification discloses that T cell co-stimulation is thought to be provided by one or more distinct cell surface molecules expressed by APC, and is thought to involve binding of co-stimulatory molecules on the surface of APC to a corresponding T cell ligand (page 3 at lines 30-33 and continuing on to page 4 at lines 1-10). The specification discloses that B7 is one co-stimulatory molecule for T cells and is a counter receptor for CD28 and CTLA-4 (page 4 at lines 11-23), and that two additional receptors related to B7 (B7-1), are B7-2 and B7-3 (page 5 at lines 5-8). The specification further discloses along with B7-1, B7-2, B7-3, that B7H, ICAM1, ICAM2, ICAM 3, LFA1, LFA2 and LFA3 are co-stimulatory molecules (especially page 7 at lines 17 and 18). The specification discloses immunizing mice with a peptide antigen emulsion, i.e., an HPV E7 peptide, followed by an intradermal injection of B7-encoding DNA plasmid vector (especially Example 1). The specification further discloses measuring CTL extracted, i.e., ex vivo, from the said mice for immunoreactivity to the E7 immunizing peptide and an increased effect when B7-encoding DNA plasmid vector was coordinately administered with the peptide antigen. The instant specification does not disclose treatment of subjects with peptide antigens other than the aforementioned HPV E7 peptide antigen and a non-viral vector encoding a co-stimulatory molecule other than B7.1. The specification discloses another co-stimulatory molecule, B7-H, that lacks the motif required for binding to CD28 and CTLA-4. The specification further discloses that another, B7h, also does not interact with CD28 and CTLA-4 and is expressed in unstimulated B cells, unlike B7.1 and B7.2 which are constitutively expressed on dendritic cells and on activated monocytes, macrophages, B cells and T cells (admitted prior art disclosed on page 27 at lines 11-30).

The specification does not disclose the definition of "B7 co-stimulatory molecule".

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as " B7 co-stimulatory molecule" without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of being able to bind to a lymphocyte ligand and provide a second signal for optimal stimulation of the primary antigen specific signal. It does not specifically define any of the molecules that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others, other than that they bind to a lymphocyte ligand of undisclosed structure. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by the property of binding to an undisclosed lymphocyte ligand and

providing a second signal does not suffice to define the genus because it is only an indication of what the property B7 co-stimulatory molecule has. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

The instant disclosure of B7-1, B7-2, B7-3 and B7H does not adequately describe the scope of the claimed invention, which encompasses a substantial variety of subgenera. Since the disclosure fails to provide sufficient relevant identifying characteristics that identify members of the genus, and given the broad genus claimed, the disclosure of a few molecules of defined sequence is insufficient to describe the claimed genus.

Applicant's arguments in the amendment filed 8/10/04 have been fully considered but are not persuasive.

Applicant's arguments are of record in the said amendment, briefly, that the amino acid sequence of a number of B7 co-stimulatory molecules were known and are described in the specification, and regions of homology between these members had been designated, and further that B7 refers to a family of surface receptors that were well-known in the art at the time of filing the instant application, having particular structural and functional characteristics, including binding with CD28 and CTLA-4 on T cells.

It is the Examiner's position that the limitation "B7 co-stimulatory molecule" is not defined in the specification. It is the Examiner's further position that although B7-1, B7-2, B7-3 and B7-H1 are disclosed in the instant specification, and they have a certain low degree of homology (about 20%) between them, they do not bind to the same ligands, i.e., B7-1, B7-2 and B7-3 bind to CD28 and CTLA-4, whereas B7-H lacks the motif required for binding to CD28 and CTLA-4. Another, B7h, also does not interact with CD28 and CTLA-4 and is expressed in unstimulated B cells, unlike B7.1 and B7.2 which are constitutively expressed on dendritic cells and on activated monocytes, macrophages, B cells and T cells (admitted prior art disclosed on page 27 at lines 11-30).

4. Claims 1, 2, 6-8 and 11-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

The specification does not disclose how to elicit an immune response in a subject comprising administering a peptide or protein antigen, including from an HIV protein, comprising one or more T cell epitopes coordinately with a non-viral vector comprising a polynucleotide encoding a B7 co-stimulatory molecule recited in the instant claims. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claim encompasses a method of eliciting an immune response where down-regulating an immune response may occur, or of treating HIV.

The specification discloses that a secondary "co-stimulation" signal is required for optimal stimulation and effective antigen specific clonal expansion of lymphocytes in addition to a primary antigen specific signal, and that a two signal model has been proposed for all lymphocytes (page 3 at lines 14-19). The specification discloses that the primary activation signal typically involves and antigenic peptide bound to either class I or class II MHC (page 3 at lines 20-22). The specification discloses that T cell co-stimulation is thought to be provided by one or more distinct cell surface molecules expressed by APC, and is thought to involve binding of co-stimulatory molecules on the surface of APC to a corresponding T cell ligand (page 3 at lines 30-33 and continuing on to page 4 at lines 1-10). The specification discloses that B7 is one co-stimulatory molecule for T cells and is a counter receptor for CD28 and CTLA-4 (page 4 at lines 11-23), and that two additional receptors related to B7 (B7-1), are B7-2 and B7-3 (page 5 at lines 5-8). The specification further discloses along with B7-1, B7-2, B7-3, that B7H, ICAM1, ICAM2, ICAM 3, LFA1, LFA2 and LFA3 are co-stimulatory molecules (especially page 7 at lines 17 and 18). The specification discloses another co-stimulatory molecule, B7-H,that lacks the motif required for binding to CD28 and CTLA-4. The specification further discloses that another, B7h, also does not interact with CD28 and CTLA-4 and is expressed in unstimulated B cells, unlike B7.1 and B7.2 which are constitutively expressed on dendritic cells and on activated monocytes, macrophages, B cells and T cells (admitted prior art disclosed on page 27 at lines 11-30). The specification does not disclose the definition of "B7 co-stimulatory molecule".

The specification discloses immunizing mice with a peptide antigen emulsion, i.e., an HPV E7 peptide, followed by an intradermal injection of B7-encoding DNA plasmid vector (especially Example 1). The specification further discloses measuring CTL extracted, i.e., ex vivo, from the said mice for immunoreactivity to the E7 immunizing peptide and an increased effect when B7-encoding DNA plasmid vector was coordinately administered with the peptide antigen. The instant specification does not disclose treatment of subjects with peptide antigens other than the aforementioned HPV E7 peptide antigen and a non-viral vector encoding a co-stimulatory molecule other than B7.1.

Evidentiary reference Rafiee et al (Cancer Gene Therapy 8(12): 974-981, 2001) teach that combined therapy, i.e., co-delivery of signal one (antigen or antigenic CTL epitope peptide) and signal two (B7.1), led to a pooper outcome than that achieved by immunotherapy with antigen or antigenic CTL epitope peptide alone, as did a time delay in administering B7.1 following antigen administration. Rafiee et al also teach that T-cell co-stimulation and antigen presentation are known to be dose-dependent, and that a strong signal one does not require signal two, and in fact, inhibition of signal two in the presence of a strong signal one can actually enhance T-cell stimulation. Rafiee et al also teach that for signal two to be effective, it must be delivered in the presence of a weak signal one (especially column 1 on page 980).

Evidentiary reference PROMT Accession No. 1998: 555242 (Lancet 24 Oct. 1998, pp 1323(1)) teaches virus variability is an important problem facing HIV vaccine researchers, that researchers have very little idea about what constitutes protective immunity, which animal model is best suited to test vaccine candidates, and that the gap between a vaccine candidate and product development remains vast, and ethical concerns surrounding clinical trials have yet to be resolved

There is insufficient guidance in the specification as to how to practice the method of the instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

Applicant's arguments in the amendment filed 7/17/03 are moot in light of the new rejection set forth above.

However, with regard to Applicant's arguments to evidentiary reference 555242, Applicant's position is of record in the said amendment on pages 8-13, briefly that the instant rejection is allegedly thrust at an alleged lack of utility and therefore, an alleged lack of "how to use" due to the inability to obtain the elicitation of a protective immune response to HIV, that the at least one asserted utility for the invention is the supplementation and enhancement of a peptide-based immunogen, that the skilled artisan would accept that coordinate administration of a non-viral vector encoding By with a protein or peptide antigen comprising one or more T cell epitopes from HIV would enhance immune recognition to that antigen, that such enhancement would be useful for killing HIV virus in an immunized individual, whether or not full elimination or indefinite containment of the HIV virus is achieved, that evidentiary reference Letvin teaches that HIV subunit vaccines elicit modest antibody responses which does not suggest that the claimed methods would not be useful for enhancing humoral immune response by further eliciting T cell help, that Letvin teaches impressive early CTL control of replicating virus and clinical protection observed prior to escape from CTL recognition due to accumulated virus mutations, that reference 555242 teaches problems in eliciting a protective immune response.

With respect to Applicant's arguments to evidentiary reference 555242, it is the Examiner's position that virus variability does preclude enhancement of an immune response to a peptide or protein composition if the isolate used to design the peptide or protein composition varies from the clinical isolate currently replicating in vivo, and that clinical testing in humans is not the issue with regard to virus variability.

It is noted that enablement must be established in the specification at the time of filing and is to be commensurate in scope with the stated claims. In re Hogan and Banks, 194 USPQ 527 (1977). Former evidentiary reference, Letvin has a publication date of July 2002, a date that is post-effective filing of the instant application. Not withstanding, it is the Examiner's position that Letvin teaches that virus-specific antibody response does not play a critical role in either the chronic or early containment of HIV replication in the infected individual (page 16, column 1, last sentence of the first full paragraph), that the neutralization-sensitive domains of the virus have proven poorly immunogenic (second to last line of the next paragraph on page 16 at column 1) and that HIV appears to be controlled predominantly by cell-mediated immunity (page 16 at column 1, last paragraph). Letvin also teaches that the immunopathogenesis of AIDS suggests that HIV is unique in its biology and may therefore not be amenable to control by immune responses elicited through traditional vaccine modalities (page 16 at paragraph 2, column 2).

In addition, it is the Examiner's position in response to Applicant's argument "that the skilled artisan reading the specification would understand that supplementation and enhancement of a peptide-based immunogen simply requires an increased immune response to the peptide antigen using the claimed methods (including co-administration of a non-viral vector encoding a B7 co-stimulatory molecule), relative to an immune response elicited in the absence of these methods", that the claims are drawn to a B7 co-stimulatory molecule such as B7-1, B7-2, B7-3 and B7-H recited in claim 11, and as such, CTL responses are what are enhanced.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites the limitation "non-viral vector encoding one or more B7 co-stimulatory molecules" in line 2. There is insufficient antecedent basis for this limitation in the claim.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 2, 6-8 and 11-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,942,607 (IDS reference) in view of Kaufmann et al (Cell. Immunol. 1996, 169/2 246-251, of record), admitted prior art in the specification on page 37 at lines 7-18, Rock et al (PNAS USA 89: 8918-8922, 1992, IDS reference), U.S. Patent No. 5,738,852 (cited previously) and WO 98/04705 and the CAPLUS Accession No. 1998: 106018 summary of the said document (both previously provided).

U.S. Patent No. 5,942,607 discloses using nucleic acid molecules encoding B7 co-stimulatory molecules such as B7-1, B7-2 or B7-3 to enhance the immunogenicity of a mammalian cell such as an APC, by transfecting the said cells with the said nucleic acid molecules and pulsing with an appropriate peptide or protein pathogen-related antigen to enhance T cell activation and immune stimulation. U.S. Patent No. 5,942,607 discloses transfecting mammalian cells with a suitable expression vector comprising a gene encoding a B7-2 (or B7-1 or B7-3) antigen ex vivo and then introducing the transfected cells into the host animal, including human, or alternatively, transfecting mammalian cells with the gene in vivo via gene therapy techniques. U.S. Patent No. 5,942,607 discloses administering therapeutically active amounts by injection such as via subcutaneous or intravenous routes. U.S. Patent No. 5,942,607 discloses use of the nucleic acid molecules encoding B7-1, B7-2 or B7-3 in anti-viral therapy to activate and generate $CD8^+$ CTL. U.S. Patent No. 5,942,607 discloses cDNA or RNA encoding B7 co-stimulatory molecules. U.S. Patent No. 5,942,607 discloses pharmaceutical carriers (especially column 3 at lines 34-60, column 15 at lines 46-62, column 18 at lines 23-24 and lines 66-67, column 19 at lines 1-18, column 20 at lines 10-33, and Abstract).

U.S. Patent No. 5,942,607 does not disclose in vivo administration of a *non-viral vector* comprising a nucleic acid molecule encoding a B7 co-stimulatory molecule coordinately---simultaneously, or separately and sequentially---with a peptide or protein antigen comprising one or more T cell epitopes, including wherein the peptide antigen comprises at least nine contiguous amino acid residues of an HPV antigenic protein.

Kaufman et al teach that HPV E7 expressing cells fail to induce an effective CTL response due to a lack of expression of co-stimulatory molecules such as CD80 (B7.1). Kaufman et al teach that introduction and expression of B7.1 gene in cervical carcinoma cells expressing HPV E7 renders the cells more immunogenic, that CTL induced against the said cells can lyse the parental tumor cells and that it is expected that these CTL will specifically lyse the tumor cells in vivo.

The prior art admission in the specification on page 37 at lines 7-18 is that direct injection of naked DNA expression vectors into vertebrate tissues has been shown to result in the uptake of DNA and long-term expression of the protein encoded by the DNA. Applicant discloses the prior art references at lines 14-18. One of the said prior art references, Fynan et al teach that epidermal, mucosal, intramuscular and intravenous routes of administration can be used for DNA vaccines (especially Discussion section).

Rock et al teach that peptides of optimal length that bind to class I MHC molecules are 8-10 amino acid residues, i.e., they may be $CD8^+$ CTL epitopes if they are recognized by the said CTL.

U.S. Patent No. 5,738,852 discloses inducing partial immunity by administering recombinant polynucleotides, including in the form of non-viral vectors or naked DNA or RNA operably linked to regulatory elements for expression, encoding immunostimulatory factor such as B7.1 and/or a target antigen polypeptide from a viral protein (entire document, especially Abstract, claims, column 4 at lines 45-67, column 6 at lines 31-32, column 9 at lines 40-46, column 10 at lines 36-46, column 13 at lines 41-67. U.S. Patent No. 5,738,852 discloses administration by any suitable means known in the art including by parenteral means, i.e., such as "subcutaneous" recited in instant claim 15. U.S. Patent No. 5,738,852 discloses that separate polynucleotides can encode the antigenic polypeptide and the co-stimulatory molecule, each is mixed with a suitable excipient and the number and timing of doses is determined by routine methods known to those of skill in the art.

WO 98/04705 and the CAPLUS Accession No. 1998: 106018 summary of the said document teach a pharmaceutical composition for treating a HPV infection comprising HPV E7 polypeptides and a co-stimulatory molecule B7.1 or a recombinant vector encoding the polypeptides.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the co-stimulatory molecule(s) disclosed by U.S. Patent No. 5,942,607, U.S. Patent No. 5,738,852, and taught by Kaufman et al, WO 98/04705 and CAPLUS Accession No. 1998: 106018 in vivo as a nucleic acid molecule as disclosed by U.S. Patent No. 5,942,607 in the form of a non-viral vector such as those taught by the prior art admitted references disclosed in the instant specification on page 37 at lines 7-18, including as taught by Fynan et al, and as disclosed by U.S. Patent No. 5,738,852, either simultaneously or separately and sequentially with a polypeptide antigen(s) as disclosed by U.S. Patent No. 5,942,607 in order to "pulse" the in vivo APC with antigen as disclosed by U.S. Patent No. 5,942,607, said antigen such as the HPV E7 polypeptide taught by Kaufman et al or the pathogen-related antigen(s) disclosed by U.S. Patent No. 5,942,607, and to administer them as peptides that comprise CTL epitopes of 8-10 amino acid residues as taught by Rock et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to enhance CTL response because U.S. Patent No. 5,942,607 discloses that co-stimulatory molecules can be administered in vivo as nucleic acid molecules that encode them and the APC are to be pulsed with antigen in order to enhance immune response via $CD8^+$ CTL, Kaufman et al teach that HPV E7 expressing cells fail to induce an effective CTL response due to a lack of expression of co-stimulatory molecules such as CD80 (B7.1), and the prior art admission in the specification teaches that direct injection of naked DNA expression vectors into vertebrate tissues has been shown to result in the uptake of DNA and long term expression of the protein encoded by the DNA, and Fynan et al teach multiple routes of administration can be used to administer DNA vaccines; WO 98/04705 and the CAPLUS Accession No. 1998: 106018 teach and U.S. Patent No. 5,738,852 discloses pharmaceutical compositions comprising B7 co-stimulatory molecules or nucleic acid molecules encoding them, and U.S. Patent No. 5,738,852 discloses inducing partial immunity by administering recombinant polynucleotides, including in the form of non-viral vectors or naked DNA or RNA operably linked to regulatory elements for expression.

With regard to the inclusion of claim 8 in the instant rejection, the minimal peptide epitope that binds to an HLA class I molecule to induce a CTL response is from 8-10 amino acid residues in length as taught by Rock et al. For example, peptides that bind to a common MHC class I molecule in humans, HLA-A2.1, are of minimal length 9 amino acid residues. Instant claim 15 is included in this rejection because it would have been prima facie obvious at the time the invention was made to have administered the antigen and polynucleotide "to proximal target sites selected from the same, or closely adjacent...sites" depending upon what route was desired. In addition, the limitation "closely adjacent" can be broadly interpreted to read on sites of undetermined distance.

Applicant's arguments in Applicant's amendment filed 8/10/04 are moot in light of this new rejection.

9. The references crossed out in the Form 1449 filed 8/10/04 have been crossed out because they were previously considered.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Wednesday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
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November 17, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600